These results indicate that UCP3 influences whole animal metabolism and, at the same time, it can be considered one of the molecular determinant of the metabolic adaptations induced by T3.

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5P8

Uncoupling protein UCP3 up-regulation during cardioplegia-induced ischemia in the human heart

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Uncoupling proteins (UCPs) comprise a subfamily of mitochondrial inner membrane anion carriers that regulate the membrane proton conductance [1]. Although their physiological function is still not established, extensive evidence indicates that they protect against free radical production and oxidative stress [1, 2]. In addition, hypoxia up-regulates UCP3 in skeletal muscle [3] and both UCP2 and UCP3 might confer cardiac ischemia tolerance [4]. Since reactive oxygen species (ROS) also increase during hypoxia [5], the increase in UCP3 could represent a mechanism aimed at decreasing oxidative damage in these conditions. Our aim was to study the effect of cardioplegic arrest-induced ischemia on the expression levels of UCP2 and UCP3 in the human heart. Cardiac biopsies from the left ventricle were obtained from patients undergoing valve replacement surgery with cardiopulmonary bypass. Biopsies were taken before and 20 or 30 min after the infusion of cardioplegic solution. UCP2 and UCP3 mRNA and protein expression levels were determined by quantitative PCR and immunoblot, respectively. UCP3 expression (mRNA and protein) increased during ischemia whereas UCP2 remained unchanged. Ischemia also induced the phosphorylation of ATF-1 (active transcription factor 1) and the nuclear accumulation of the antioxidant transcription factor Nrf2 (NF-E2-related factor 2). Consequently, the mRNA levels of several Nrf2 target genes were also induced. On the contrary, HIF (hypoxia inducible factor) sensitive genes did not change. Relative levels of the five mitochondrial OXPHOS complexes were similar before and after ischemia. Pearson correlation coefficients indicated a positive correlation between UCP3 and Nrf2. The up-regulation of UCP3 during cardiac ischemia could represent a cardioprotective mechanism of mitochondrial depolarization aimed at limiting ROS production.

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5P9

Upregulation of mitochondrial glycerol-3-phosphate dehydrogenase abundance in brown adipose tissue mitochondria from UCP1 knock-out mice

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Uncoupling protein 1 (UCP1) is a mitochondrial inner membrane protein that facilitates heat production in brown adipose tissue and is central to the process of non-shivering thermogenesis in mammals. Furthermore, UCP1 has been demonstrated to have the potential to regulate reactive oxygen containing species (ROS) production by brown adipose tissue mitochondria. One of the crucial sources of electrons for the electron transport chain in brown adipose tissue is via mitochondrial glycerol-3-phosphate dehydrogenase. Mitochondrial glycerol-3-phosphate dehydrogenase is part of the glycerol-phosphate shuttle and links cytoplasmic glycolysis to mitochondrial oxidative phosphorylation. Interestingly, UCP1 knock-out mice showed (a) significantly increased (1.6-fold, $p<0.01$) oxygen consumption rates in brown adipose tissue mitochondria when respiring on glycerol-3-phosphate, (b) increased glycerol-3-phosphate dehydrogenase enzymic activity (1.6-fold, $p<0.001$) and (c) increased abundance of mitochondrial glycerol-3-phosphate dehydrogenase (3-fold, $P=0.003$) per unit mass of mitochondria compared to wild-type controls. Subsequent work will seek to explain the apparent reciprocal arrangement between lack of UCP1 and increased mitochondrial glycerol-3-phosphate dehydrogenase abundance/activity.

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Molecular characterization of brown adipose tissue in a 'protoendothermic' mammal provides a novel approach to the understanding of uncoupling protein evolution

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The molecular events that facilitated the evolutionary transition from ecto- to endothermia in vertebrates are still unknown. The 'ancient' Lesser hedgehog tenrec, *Echinops telfairi* is considered a 'protoendothermic' mammal as it shows fluctuating, ectothermic-like body temperature patterns. Interestingly, females maintain constantly high body temperatures (~33 °C) during pregnancy and periods of parental care, demonstrating regulatory heat production. Thus, understanding the thermophysiology of this 'protoendotherm' may help to elucidate ancient patterns that led to 'modern'(sustained) endothermy.

We searched for, and characterized the molecular basis of NST in warm (27 °C) and cold (20 °C) acclimated *E. telfairi in vivo* and *in vitro*. Administration of a selective ß3-AR antagonist suppressed rewarming rates from torpor after cold acclimation, indicating involvement of adrenergically mediated nonshivering thermogenesis (NST). Next, morphological analysis revealed a BAT-like depot. The proton leak of isolated BAT mitochondria could be inhibited by GDP, suggesting UCP1-dependent proton conductance and, hence,